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Links

MILK FAT GLOBULE-EGF FACTOR 8; MFGE8**Alternative titles; symbols****LACTADHERIN
MEDIN, INCLUDED**

Gene map locus 15q25

TEXT**CLONING**

Stubbs et al. (1990) identified a cDNA for a mouse mammary epithelial cell surface protein, which they called milk fat globule-EGF factor 8 (MFGE8) because of its regions of sequence similarity to epidermal growth factor (EGF) and blood clotting factors VIII (306700) and V (227400). Larocca et al. (1991) raised monoclonal antibodies to a 46-kD human milk fat globule protein, later to be identified as the human homolog of MFGE8, and isolated a partial cDNA by immunoscreening a lambda gt11 human breast cDNA library. Collins et al. (1997) cloned the MFGE8 gene from a human infant cDNA brain library. The gene predicts a protein of 387 amino acids of which 263 (68%) are identical or conserved matches with the mouse protein. Ⓢ

Medin

Aortic medial amyloid is a form of localized amyloid that occurs in virtually all individuals older than 60 years. Haggqvist et al. (1999) purified a 5.5-kD aortic medial amyloid component by size-exclusion chromatography and reversed phase-HPLC from 3 individuals, and showed by amino acid sequence analysis that the amyloid is derived from an integral proteolytic fragment of lactadherin. Lactadherin is a 364-amino acid glycoprotein known to be expressed by mammary epithelial cells as a cell surface protein and secreted as part of the milk fat globule membrane (Larocca et al., 1991; Aoki et al., 1997). The multidomain protein has a C-terminal domain showing homology to blood coagulation factors V and VIII. They found that the main constituent of aortic medial amyloid is a 50 amino acid-long peptide, designated medin by Haggqvist et al. (1999), that is positioned within the coagulation factor-like domain of lactadherin. This result was supported by the specific labeling of aortic medial amyloid in light and electron microscopy with 2 rabbit antisera raised against 2 synthetic peptides corresponding to different parts of medin. Using in situ hybridization, they showed that lactadherin is expressed by aortic medial smooth muscle cells. Furthermore, one of the synthetic peptides formed amyloid-like fibrils in vitro. Lactadherin had not been known to be an amyloid precursor protein or to be expressed in aortic tissue.

Homology of lactadherin with other proteins implicated its involvement in important cell surface-mediated regulatory events. ⚡

MAPPING

By fluorescence in situ hybridization, Collins et al. (1997) mapped the MFGE8 gene to chromosome 15q25.

GENE FUNCTION

Hanayama et al. (2002) found that MFGE8 is a factor that links apoptotic cells to phagocytes. MFGE8 specifically bound to apoptotic cells by recognizing aminophospholipids such as phosphatidylserine. MFGE8, when engaged by phospholipids, bound to cells via its RGD (arg-gly-asp) motif. It bound particularly strongly to cells expressing alpha-V-beta-3 integrin (see 193210). The NIH3T3 cell transformants that expressed a high level of alpha-V-beta-3 integrin engulfed apoptotic cells when MFGE8 was added. MFGE8 carrying a point mutation in the RGD motif behaved as a dominant-negative form, and inhibited the phagocytosis of apoptotic cells by peritoneal macrophages in vitro and in vivo. Hanayama et al. (2002) concluded that MFGE8 secreted from activated macrophages binds to apoptotic cells and brings them to phagocytes for engulfment. ⚡

REFERENCES

1. Aoki, N.; Ishii, T.; Ohira, S.; Yamaguchi, Y.; Negi, M.; Adachi, T.; Nakamura, R.; Matsuda, T. : **Stage specific expression of milk fat globule membrane glycoproteins in mouse mammary gland: comparison of MFG-E8, butyrophilin, and CD36 with a major milk protein, beta-casein.** *Biochim. Biophys. Acta* 1334: 182-190, 1997.
PubMed ID : 9101712
2. Collins, C.; Nehlin, J. O.; Stubbs, J. D.; Kowbel, D.; Kuo, W.-L.; Parry, G. : **Mapping of a newly discovered human gene homologous to the apoptosis associated-murine mammary protein, MFG-E8, to chromosome 15q25.** *Genomics* 39: 117-118, 1997.
PubMed ID : 9027496
3. Haggqvist, B.; Naslund, J.; Sletten, K.; Westermark, G. T.; Mucchiano, G.; Tjernberg, L. O.; Nordstedt, C.; Engstrom, U.; Westermark, P. : **Medin: an integral fragment of aortic smooth muscle cell-produced lactadherin forms the most common human amyloid.** *Proc. Nat. Acad. Sci.* 96: 8669-8674, 1999.
PubMed ID : 10411933
4. Hanayama, R.; Tanaka, M.; Miwa, K.; Shinohara, A.; Iwamatsu, A.; Nagata, S. : **Identification of a factor that links apoptotic cells to phagocytes.** *Nature* 417: 182-187, 2002.
PubMed ID : 12000961
5. Larocca, D.; Peterson, J. A.; Urrea, R.; Kuniyoshi, J.; Bistrain, A. M.; Ceriani, R. L. : **A M(r) 46,000 human milk fat globule protein that is highly expressed in human breast tumors contains factor VIII-like domains.** *Cancer Res.* 51: 4994-4998, 1991.
PubMed ID : 1909932
6. Stubbs, J. D.; Lekutis, C.; Singer, K. L.; Bui, A.; Yuzuki, D.; Srinivasan, U.; Parry, G. :

cDNA cloning of a mouse mammary epithelial cell surface protein reveals the existence of epidermal growth factor-like domains linked to factor VIII-like sequences. *Proc. Nat. Acad. Sci.* 87: 8417-8421, 1990.
PubMed ID : 2122462

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aliphatic

<[biochemistry](#), [chemistry](#)> A [major class](#) of [organic compounds](#) where [carbon](#) and [hydrogen molecules](#) are arranged in [straight](#) or branched [chains](#).

A [type](#) of [hydrocarbon](#) that includes [alkanes](#), [alkenes](#), and [alkynes](#).

(13 Nov 1997)

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